

established, it shall be allowed an initial dating period equal to the dating of the product or as supported by data acceptable to APHIS, except that frozen references may have an initial dating period of 5 years, or as supported by data acceptable to APHIS. Prior to the expiration date, such reference may be granted an extension of dating by confirming its immunogenicity using a Qualifying Serial of product.

(e) Final container samples of completed product derived from Master Seed found immunogenic in accordance with paragraph (a) of this section and found satisfactory in accordance with paragraphs (b) and (c) of this section may also be subjected to an animal potency test by Animal and Plant Health Inspection Service as provided in this paragraph. Products shall be used according to label directions including dose(s) and route of administration.

(1) A one stage test using 20 vaccinates and 5 controls or a two stage test using 10 vaccinates and 5 controls for each stage shall be used. The criteria used for judging the specific response in the controls and vaccinates shall be in accordance with the test protocol used in the Master Seed immunogenicity test.

(2) If at least 80 percent of the controls do not show specific responses to challenge, the test is inconclusive and may be repeated. If a vaccinate shows the specific responses to challenge expected in the controls, the vaccinate shall be listed as a failure.

(3) The results of the testing shall be evaluated according to the following table:

CUMULATIVE TOTALS			
Stage	Number of animals	Failures for satisfactory serials	Failures for unsatisfactory serials
1	10	1 or less	3 or more.
2 (or 1)	20	4 or less	5 or more.

(4) When a serial has been found unsatisfactory for potency by the test provided in paragraphs (e)(1), (2), and (3) of this section, the serial shall be withheld from the market and the following actions taken:

(i) The Administrator shall require that at least two additional serials prepared with the same Master Seed be

subjected to similar animal potency tests by Animal and Plant Health Inspection Service or the licensee or both.

(ii) If another serial is found unsatisfactory for potency, the product shall be removed from the market while a reevaluation of the product is made and the problem is resolved.

[49 FR 22625, May 31, 1984, as amended at 56 FR 66784, 66786, Dec. 26, 1991; 62 FR 19038, Apr. 18, 1997; 72 FR 72564, Dec. 21, 2007]

§ 113.9 New potency test.

A potency test written into the filed Outline of Production for a product shall be considered confidential information by Animal and Plant Health Inspection Service until at least two additional product licenses are issued for the product or unless use of the test is authorized by the licensee, in which case, such potency test may be published as part of the Standard Requirement for the product.

(a) Until a potency test is published as part of the Standard Requirement for the product, reference to such a test shall be made in the filed Outline of Production and the test shall be conducted.

(b) When a potency test has been published as part of the Standard Requirement, such test shall be conducted unless the product is specifically exempted as provided in § 113.4.

[40 FR 14084, Mar. 28, 1975, as amended at 56 FR 66784, Dec. 26, 1991]

§ 113.10 Testing of bulk material for export or for further manufacture.

When a product is prepared in a licensed establishment for export in large multiple-dose containers as provided in § 112.8(d) or (e) of this subchapter or for further manufacturing purposes as provided in § 114.3(d) of this subchapter, samples of the bulk material shall be subjected to all required tests prescribed in the filed Outline of Production or Standard Requirements for the product. Samples of concentrated liquid product shall be diluted to a volume equal to the contents of the sample times the concentration factor prior to initiating potency tests.

[49 FR 45846, Nov. 21, 1984]

§ 113.25

STANDARD PROCEDURES

§ 113.25 Culture media for detection of bacteria and fungi.

(a) Ingredients for which standards are prescribed in the United States Pharmacopeia, or elsewhere in this part, shall conform to such standards. In lieu of preparing the media from the individual ingredients, they may be made from dehydrated mixtures which, when rehydrated with purified water, have the same or equivalent composition as such media and have growth-promoting buffering, and oxygen tension-controlling properties equal to or better than such media. The formulas for the composition of the culture media prescribed in §§113.26 and 113.27 are set forth in the United States Pharmacopeia, 19th Edition.

(b) The licensee shall test each quantity of medium prepared at one time from individual ingredients and the first quantity prepared from each lot of commercial dehydrated medium for growth-promoting qualities. If any portion of a lot of commercial dehydrated medium is held for 90 days or longer after being so tested, it shall be retested before use. Two or more strains of micro-organisms that are exacting in their nutritive requirements shall be used. More than one dilution shall be used to demonstrate the adequacy of the medium to support the growth of a minimum number of micro-organisms.

(c) The sterility of the medium shall be confirmed by incubating an adequate number of test vessels and examining each for growth. Additional control may be used by incubation of representative uninoculated test vessels for the required incubation period during each test.

(d) A determination shall be made by the licensee for each biological product of the ratio of inoculum to medium which shall result in sufficient dilution of such product to prevent bacteriostatic and fungistatic activity. The determination may be made by tests on a representative biological product for each group of comparable products containing identical preservatives at equal or lower concentrations. Inhibitors or neutralizers of preservatives, approved by the Administrator,

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may be considered in determining the proper ratio.

[35 FR 16039, Oct. 13, 1970, as amended at 37 FR 2430, Feb. 1, 1972; 41 FR 27715, July 6, 1976; 56 FR 66784, Dec. 26, 1991]

§ 113.26 Detection of viable bacteria and fungi except in live vaccine.

Each serial and subserial of biological product except live vaccines shall be tested as prescribed in this section unless otherwise specified by the Administrator. When cell lines, primary cells, or ingredients of animal origin used in the preparation of a biological product are required to be free of viable bacteria and fungi, they shall also be tested as prescribed in this section.

(a) The media to be used shall be as follows:

(1) Fluid Thioglycollate Medium with 0.5 percent beef extract shall be used to test for bacteria in biological products containing clostridial toxoids, bacterins, and bacterin-toxoids.

(2) Fluid Thioglycollate Medium with or without 0.5 percent beef extract shall be used to test for bacteria in biological products other than clostridial toxoids, bacterins, and bacterin-toxoids.

(3) Soybean-Casein Digest Medium shall be used to test biological products for fungi; provided, that Fluid Thioglycollate Medium without beef extract shall be substituted when testing biological products containing mercurial preservatives.

(b) Test procedure:

(1) Ten test vessels shall be used for each of two media selected in accordance with paragraph (a)(1), (a)(2), or (a)(3) of this section. Each test vessel shall contain sufficient medium to negate the bacteriostatic or fungistatic activity in the inoculum as determined in §113.25(d).

(2) Inoculum:

(i) When completed product is tested, 10 final container samples from each serial and each subserial shall be tested. One ml from each sample shall be inoculated into a corresponding individual test vessel of culture medium: *Provided, That*, if each final container sample contains less than 2 ml, one-half of the contents shall be used as inoculum for each test vessel.